

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Atty. Docket No: MSA-004.01

In re patent application of

Duff, Gordon W. et al.

Serial No. 09/247,874

Filed: February 10, 1999

For: THERAPEUTIC AND DIAGNOSTIC BASED ON A NOVEL IL-1B MUTATION

STATEMENT TO SUPPORT FILING AND SUBMISSION IN  
ACCORDANCE WITH 37 C.F.R. §§ 1.821-1.825

Assistant Commissioner for Patents  
Washington, D.C. 20231  
**Box SEQUENCE**

Sir:

In connection with a Sequence Listing submitted concurrently herewith, the undersigned hereby states that:

1. the submission, filed herewith in accordance with 37 C.F.R. § 1.821(g), does not include new matter;

2. the content of the attached paper copy and the attached computer readable copy of the Sequence Listing, submitted in accordance with 37 C.F.R. § 1.821(c) and (e), respectively, are the same; and

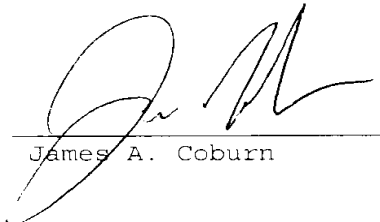
3. all statements made herein of their own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United

Serial No. 09/247,874

States Code and that such willful false statements may jeopardize the validity of the application or any patent resulting therefrom.

Respectfully submitted,

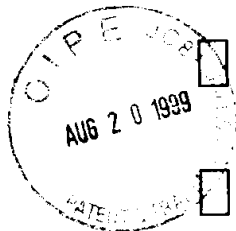
Aug. 19, 1999  
Date

  
James A. Coburn

**HARBOR CONSULTING**  
Intellectual Property Services  
1500A Lafayette Road  
Suite 262  
Portsmouth, N.H.  
800-318-3021

**NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING  
NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES**

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):



- ☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.
- ☒ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- ☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- ☒ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- ☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- ☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- ☐ 7. Other: \_\_\_\_\_

**Applicant Must Provide:**

- ☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- ☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- ☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216

For CRF Submission Help, call (703) 308-4212

PatentIn Software Program Support (SIRA)

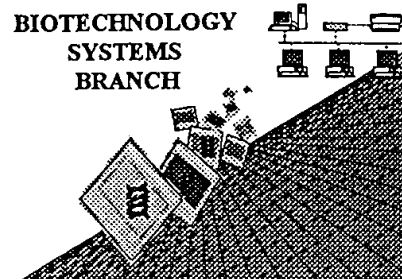
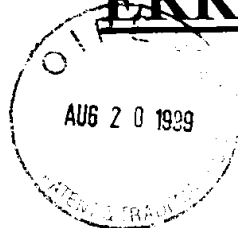
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To Purchase PatentIn Software.....703-306-2600

**PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR RESPONSE**

R. Schnizer

# **RAW SEQUENCE LISTING** **ERROR REPORT**



The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following CRF diskette:

Application Serial Number:

09/247,874

Art Unit / Team No. :

1632

Date Processed by STIC:

6/15/99

**THE ATTACHED PRINTOUT EXPLAINS THE ERRORS DETECTED.**

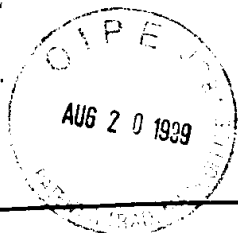
**PLEASE BE SURE TO FORWARD THIS INFORMATION TO THE APPLICANTS BY EITHER:**

- 1) INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE APPLICANTS ALONG WITH A NOTICE TO COMPLY or,**
- 2) CALLING APPLICANTS AND FAXING THEM A COPY OF THE PRINTOUT WITH A NOTICE TO COMPLY**

**THIS WILL INSURE THAT THE NEXT SUBMISSION RECEIVED FROM THEM WILL BE ERROR FREE.**

**IF YOU HAVE ANY FURTHER QUESTIONS, PLEASE CALL:**

**ARTI SHAH 703-308-4212**



## Raw Sequence Listing Error Summary

**ERROR DETECTED SUGGESTED CORRECTION**

SERIAL NUMBER: 09/247,874

ATTN: NEW RULES CASES: PLEASE DISREGARD ENGLISH "ALPHA" HEADERS, WHICH WERE INSERTED BY PTO SOFTWARE

- 1        Wrapped Nucleics      The number/text at the end of each line "wrapped" down to the next line.  
This may occur if your file was retrieved in a word processor after creating it.  
Please adjust your right margin to .3, as this will prevent "wrapping".
- 2        Wrapped Aminos      The amino acid number/text at the end of each line "wrapped " down to the next line.  
This may occur if your file was retrieved in a word processor after creating it.  
Please adjust your right margin to .3, as this will prevent "wrapping".
- 3        Incorrect Line Length      The rules require that a line not exceed 72 characters in length. This includes spaces.
- 4        Misaligned Amino Acid      The numbering under each 5th amino acid is misaligned. This may be caused by the use of tabs  
Numbering      between the numbering. It is recommended to delete any tabs and use spacing between the numbers.
- 5        Non-ASCII      This file was not saved in ASCII (DOS) text, as required by the Sequence Rules.  
Please ensure your subsequent submission is saved in ASCII text so that it can be processed.
- 6        Variable Length      Sequence(s)        contain n's or Xaa's which represented more than one residue.  
As per the rules, each n or Xaa can only represent a single residue.  
Please present the maximum number of each residue having variable length and  
indicate in the (ix) feature section that some may be missing.
- 7        PatentIn ver. 2.0 "bug"      A "bug" in PatentIn version 2.0 has caused the <220>-<223> section to be missing from amino acid  
sequence(s)       . Normally, PatentIn would automatically generate this section from the  
previously coded nucleic acid sequence. Please manually copy the relevant <220>-<223> section  
to the subsequent amino acid sequence.
- 8        Skipped Sequences      Sequence(s)        missing. If intentional, please use the following format for each skipped sequence:  
(OLD RULES)      (2) INFORMATION FOR SEQ ID NO:X:  
                         (i) SEQUENCE CHARACTERISTICS:(Do not insert any headings under "SEQUENCE CHARACTERISTICS")  
                         (xi) SEQUENCE DESCRIPTION:SEQ ID NO:X:  
                         This sequence is intentionally skipped  
  
Please also adjust the "(iii) NUMBER OF SEQUENCES:" response to include the skipped sequence(s).
- 9        Skipped Sequences      Sequence(s)        missing. If intentional, please use the following format for each skipped sequence.  
(NEW RULES)      <210> sequence id number  
                         <400> sequence id number  
                         000
- 10        Use of n's or Xaa's      Use of n's and/or Xaa's have been detected in the Sequence Listing.  
(NEW RULES)      Use of <220> to <223> is MANDATORY if n's or Xaa's are present.  
In <220> to <223> section, please explain location of n or Xaa, and which residue n or Xaa represents.
- 11        Use of <213>Organism      Sequence(s)        are missing this mandatory field or its response.  
(NEW RULES)
- 12        Use of <220>Feature      Sequence(s)        are missing the <220>Feature and associated headings.  
(NEW RULES)      Use of <220> to <223> is MANDATORY if <213>ORGANISM is "Artificial" or "Unknown"  
Please explain source of genetic material in <220> to <223> section.  
(See "Federal Register," 6/01/98, Vol. 63, No. 104, pp. 29631-32) (Sec. 1.823 of new Rules)
- 13        PatentIn ver. 2.0 "bug"      Please do not use "Copy to Disk" function of PatentIn version 2.0. This causes a corrupted  
file, resulting in missing mandatory numeric identifiers and responses (as indicated on raw sequence listing).  
Instead, please use "File Manager" or any other means to copy file to floppy disk.

R. Scriver



1632

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RAW SEQUENCE LISTING  
PATENT APPLICATION US/09/247,874

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This Raw Listing contains the General Information  
Section and up to first 5 pages.

see  
P. 5 and P. 4, to

1 <110> APPLICANT: Duff, Gordon W.  
2 di Giovine, Francesco Saverio  
3 <120> TITLE OF INVENTION: THERAPEUTIC AND DIAGNOSTIC BASED ON A NOVEL IL-1B  
4 MUTATION  
5 <130> FILE REFERENCE: MSA-004.01  
6 <140> CURRENT APPLICATION NUMBER: US/09/247,874  
7 <141> CURRENT FILING DATE: 1999-02-10  
8 <160> NUMBER OF SEQ ID NOS: 18  
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Does Not Comply  
Corrected Diskette Needed

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PATENT APPLICATION US/09/247,874

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TIME: 11:56:38

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135	ctactctcgg	ggctaggggt	tggggtgacc	ctgcatgctg	tgtccctaac	cacaagaccc	7260
136	ccttctttct	tcagtgggtg	tctccatgtc	ctttgtacaa	ggagaagaaa	gtaatgacaa	7320
137	aatacctgtg	gccttgggccc	tcaaggaaaa	gaatctgtac	ctgtcctgcg	tgttgaaaga	7380
138	tgataagccc	actctacagc	tggaggttaag	tgaatgctat	ggaatgaagc	ccttctcagc	7440
139	ctcctgctac	cacttattcc	cagacaattc	accttctccc	cgcccccatc	cctaggaaaa	7500
140	gctgggaaca	ggtctatttg	acaagttttg	cattaatgta	aataaattta	acataatttt	7560
141	taactgogtg	caaccttcaa	tctgtctgca	gaaaattaaa	tcattttgcc	gatgttatta	7620
142	tgtcctacca	tagttacaac	cccaacagat	tatatattgt	tagggctgct	ctcatttgat	7680
143	agacaccttg	ggaaatagat	gacttaaagg	gtccatttat	cacgtccact	ccactcccaa	7740
144	aatcaccacc	actatcacct	ccagctttct	cagcaaaaagc	ttcattttcca	agttgatgtc	7800



AGE: 4

# RAW SEQUENCE LISTING PATENT APPLICATION US/09/247,874

DATE: 06/15/1999  
TIME: 11:56:38

Input Set: I247874.RAW

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145 attctaggac cataaggaaa aatacaataa aaagcccctg gaaactaggt acttcaagaa 7860
146 gctctagctt aatttttcacc ccccaaaaaa aaaaaaattc tcacctacat tatgctcctc 7920
147 agcatttggc actaagtttt agaaaagaag aagggtctct ttaataatca cacagaaagt 7980
148 tgggggcccc gttacaactc aggagtctgg ctctgatca tgtgacctgc tctgcagttt 8040
149 cctttctggc caacccaaag aacatctttc ccataggcat ctttgtccct tgccccacaa 8100
150 aaattcttct ttctctttcg ctgcagagt tagatcccaa aaattaccca aagaagaaga 8160
151 tggaaaagcg atttgtcttc aacaagatag aaatcaataa caagctggaa tttgagtctg 8220
152 ccaggttccc caactggtag atcagcacct ctcaagcaga aaacatgccc gtcttcctgg 8280
153 gagggaccaa aggcggccag gatataactg acttcaccat gcaatttgtg tcttcctaaa 8340
154 gagagctgta ccagagagt cctgtgctga atgtggactc aatccctagg gctggcagaa 8400
155 agggaaacaga aaggtttttg agtacggcta tagcctggac tttcctgttg tctacaccaa 8460
156 tgcccaactg cctgccttag ggtagtgcta agaggatctc ctgtccatca gccaggacag 8520
157 tcagctctct cctttcaggg ccaatcccca gcccttttgt tgagccaggc ctctctcacc 8580
158 tctctactc acttaaagcc cgcctgacag aaaccacggc cacatttggg tctaagaaac 8640
159 cctctgtcat tctgtcccac attctgatga gcaaccgctt ccctatttat ttatttattt 8700
160 gtttgtttgt tttgattcat tggctcaatt tattcaaagg gggcaagaag tagcagtgtc 8760
161 tgtaaaagag cctagttttt aatagctatg gaatcaattc aatttggact ggtgtgctct 8820
162 ctttaaatca agtcctttta ttaagactga aaatatataa gctcagatta tttaaatggg 8880
163 aatatttata aatgagcaaa tatcatactg ttcaatgggt ctgaaataaa cttcactgaa 8940
164 gaaaaaaaaa aaagggtctc tctgatcat tgactgtctg gattgacact gacagtaagc 9000
165 aaacaggctg tgagagtctt tgggactaag cccactctc attgctgagt gctgcaagta 9060
166 cctagaaata tccttgcca ccgaagacta tctctctcac ccatccctt tatttcgttg 9120
167 ttcaacagaa ggatattcag tgcacatctg gaacaggatc agctgaagca ctgcaggagg 9180
168 tcaggactgg tagtaacagc taccatgatt tatctatcaa tgcaccaaac atctgttgag 9240
169 caagcgctat gtactaggag ctgggagtac agagatgaga acagtcacaa gtccctctc 9300
170 agataggaga ggcagctagt tataagcaga acaaggtaac atgacaagta gagtaagata 9360
171 gaagaacgaa gaggagtagc caggaaggag ggaggagaac gacataagaa tcaagcctaa 9420
172 agggataaac agaagatttc cacacatggg ctgggccaat tgggtgtcgg ttacgcctgt 9480
173 aatcccagca ctttgggtgg caggggcaga aagatcgctt gagcccagga gttcaagacc 9540
174 agcctgggca acatagttag actcccatct ctacaaaaaa taaataaata aataaaaaca 9600
175 tcagccaggc atgctggcat gcacctgtag tctagctac ttgggaagct gacactggag 9660
176 gattgcttga gcccagaagt tcaagactgc agtgagctta tccgttgacc tgcaggctga 9720
177 c 9721

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178 &lt;210&gt; SEQ ID NO 2

179 &lt;211&gt; LENGTH: 9721

180 &lt;212&gt; TYPE: DNA

181 &lt;213&gt; ORGANISM: IL-1Beta allele 2

182 &lt;400&gt; SEQUENCE: 2

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183 agaaagaaag agagagagaa agaaaagaaa gaggaaggaa ggaaggaagg aagaaagaca 60
184 ggctctgagg aaggtggcag ttctacaac gggagaacca gtggttaatt tgcaaagtgg 120
185 atcctgtgga ggcanncaga ggagtcacct agggccacca gacagggtct ttagctatct 180
186 gcaggccaga caccaaattt caggagggct cagtgttagg aatggattat ggcttatcaa 240
187 attcacagga aactaacatg ttgaacagct tttagatttc ctgtggaaaa tataacttac 300
188 taaagatgga gttcttgtga ctgactcctg atatcaagat actgggagcc aaattaaaaa 360
189 tcagaaggct gcttggagag caagtccatg aaatgctctt tttcccacag tagaacctat 420
190 ttccctctgt tctcaaatac ttgcacagag gctcactccc ttggataatg cagagcgagc 480
191 acgatacctg gcacatacta atttgaataa aatgctgtca aattcccatc caccatttca 540
192 agcagcaaac tctatctcac ctgaatgtac atgccaggca ctgtgctaga cttggctcaa 600
193 aaagatttca gtttcctgga ggaaccagga gggcaagggt tcaactcagt gctataagaa 660
194 gtgttacagg ctggacacgg tggctcacgc ctgtaatccc aacatttggg aggccgaggc 720

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AGE: 5

RAW SEQUENCE LISTING  
PATENT APPLICATION US/09/247,874

DATE: 06/15/1999  
TIME: 11:56:38

Input Set: I247874.RAW

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195   gggcagatca caaggtcagg agatcgagac catcctggct aacatggtga aaccctgtct 780
196   ctactaaaaa tacaaaaaat tagccgggag ttggcggcag gtgcctgtag tcccagctgc 840
197   tggggaggct gaggcaggag aatggtgtga acccgggagg cggaacttgc agggggccga 900
198   gatcgtgccca ctgcactcca gcctgggcca cagagtgaga ctctgtctca aaaaaaaaaa 960
199   aaaagtgtta tgatgcagac ctgtcaaaga ggcaaaggag ggtgttccta cactccaggc 1020
200   actgttcata acctggactc tcattcattc tacaaatgga gggctcccct gggcagatcc 1080
201   ctggagcagg cactttgctg gtgtctcggc taaagagaaa ctgataactc ttggtattac 1140
202   caagagatag agtctcagat ggatattctt acagaaacaa tattcccact tttcagagtt 1200
203   caccaaaaaa tcattttagg cagagctcat ctggcattga tctggttcat ccatgagatt 1260
204   ggctagggtta acagcacctg gtcttgagg gttgtgtgag cttatctcca gggttgcccc 1320
205   aactccgtca ggagcctgaa ccctgcatac cgtatgttct ctgcccagc caagaaaggt 1380
206   caattttctc ctgagaggct cctgcaattg acagagagct cccgaggcag agaacagcac 1440
207   ccaaggtaga gaccacacc ctcaatacag acaggaggag ctattggccc ttcattgtac 1500
208   ccatatatcc atctgtaagt gggaagattc ctaaacttaa gtacaaagaa gtgaatgaag 1560
209   aaaagtatgt gcatgtataa atctgtgtgt cttccacttt gtcccacata tactaaattt 1620
210   aaacattctt ctaacgtggg aaaatccagt attttaatgt ggacatcaac tgcacaacga 1680
211   ttgtcaggaa aacaatgcat atttgcattg tgatacattt gcaaaatgtg tcatagtttg 1740
212   ctactccttg cccttccatg aaccagagaa ttatctcagt ttattagtcc cctcccctaa 1800
213   gaagcttcca ccaatactct tttccccttt cctttaactt gattgtgaaa tcaggatttc 1860
214   aacagagaaa tttctcagcc tctacttctt gcttttgaaa gctataaaaa cagcgaggga 1920
215   gaaactggca gataccaaac ctcttcgagg cacaaggcac aacaggctgc tctgggattc 1980
216   tcttcagcca atcttcattg ctcaagtatg actttaatct tctttacaac taggtgctaa 2040
217   gggagtctct ctgtctctct gcctctttgt gtgtatgcac attctctctc totctctctt 2100
218   tctttctctg tctctctctt ccttctctct tgctctctct ctgagctttt tgcaaaaatg 2160
219   ccagggtgaa tataatgctt atgactcggg aaatattctg ggaatggata ctgcttatct 2220
220   aacagctgac accctaaagg ttagtgtcaa agcctctgct ccagctctcc tagccaatac 2280
221   attgctagtt ggggtttggt ttagcaaatg cttttctcta gacccaaagg acttctcttt 2340
222   cacacattca ttcatttact cagagatcat ttctttgcat gactgccatg cactggatgc 2400
223   tgagagaaat cacacatgaa cgtagccgtc atggggaagt cactcatttt ctcttttta 2460
224   cacagggtgc tgaagcagcc atggcagaag tacctgagct cgccagtga atgatggctt 2520
225   attacaggtc agtgagacg ctgagaccag taacatgagc aggtctctct tttcaagagt 2580
226   agagtgttat ctgtgcttgg agaccagatt tttcccctaa attgcctctt tcagtggcaa 2640
227   acagggtgcc aagtaaactc gatttaaaga ctactttccc attacaagtc cctccagcct 2700
228   tgggacctgg aggctatcca gatgtgttgt tgcaagggct tctgcagag gcaaatgggg 2760
229   agaaaagatt ccaagcccac aatacaagga atccctttgc aaagtgtggc ttggaggagg 2820
230   agggagagct cagattttag ctgactctgc tgggctagag gttaggcctc aagatccaac 2880
231   agggagcacc aggtgcccc cctgccaggc ctagaatctg ccttctggac tgttctgocg 2940
232   atatcactgt gaaacttgc aggtgtttca ggcagctttg agaggcaggc tgtttgcagt 3000
233   ttcttatgaa cagtcaagtc ttgtacacag ggaaggaaaa ataaacctgt ttagaagaca 3060
234   taattgagac atgtccctgt ttttattaca gtggcaatga ggatgacttg tctttgaag 3120
235   ctgatggccc taaacagatg aaggtaagac tatgggttta actcccaacc caaggaaggg 3180
236   ctctaacaca gggaaagctc aaagaaggga gttctgggac actttgatgc catggtattt 3240
237   tgtttttaga agactttaac ctcttcagc gagacacagg ctgcaccact tgctgacctg 3300
238   gccacttggt catcatatca ccacagtcac tctaactcgt tgggtggtgt ggccacactt 3360
239   ggtggtgaca ggggaggagt agtgataatg tccccatttc atagtaggaa gacaaccaag 3420
240   tcttcaacat aaatttgatt atccttttaa gagatggatt cagcctatgc caatcacttg 3480
241   agttaaactc tgaaccaag agatgatctt gagaactaac atatgtctac ccttttgag 3540
242   tagaatagtt ttttctacc tggggtgaag cttataacaa caagacatag atgatataa 3600
243   caaaaagatg aattgagact tgaagaaaa ccattcactt gctgtttgac cttgacaagt 3660
244   cattttaccc gctttggacc tcatctgaaa aataaagggc tgagctggat gatctctgag 3720

```

ase Note:

of n and/or Xaa have been detected in the Sequence Listing. Please review the  
Sequence Listing to ensure that a corresponding explanation is presented in the <220> to  
<23> fields of each sequence which presents at least one n or Xaa.

AGE: 6

VERIFICATION SUMMARY  
PATENT APPLICATION US/09/247,874

DATE: 06/15/1999  
TIME: 11:56:38

Input Set: I247874.RAW

line	? Error/Warning	Original Text
17	W "N" or "Xaa" used: Feature required	atcctgtgga ggcanncaga ggagtccctt aggccacc
185	W "N" or "Xaa" used: Feature required	atcctgtgga ggcanncaga ggagtccctt aggccacc
437	W "N" or "Xaa" used: Feature required	ccgactcgag nnnnnnatgt gg